UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/244,130	02/04/1999	BERNARD DUJON	3495.0111-10	3378

22852 7590 04/09/2003

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER LLP
1300 I STREET, NW
WASHINGTON, DC 20005

EXAMINER	
KAUSHAL, SUMESH	

ART UNIT	PAPER NUMBER
1636	

DATE MAILED: 04/09/2003

33

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/244,130	DUJON ET AL.	
	Examiner	Art Unit	
	Sumesh Kaushal Ph.D.	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *94-119* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *94-119* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's response filed on 02/05/03 has been acknowledged.

Claims 53-86 are canceled.

Claims 94-119 are newly filed.

Claims 94-119 are pending and are examined in this office action.

► *Applicants are advised to follow Amendment Practice under revised 37 CFR §1.121 (http://www.uspto.gov/web/offices/pac/dapp/opla/preognotice/revamdtprac.htm). Each amendment document that includes a change to an existing claim, or submission of a new claim,* ***must include a complete listing of all claims*** *in the application. After each claim number, the status must be indicated in a parenthetical expression, and the text of each claim under examination (with markings to show current changes) must be presented. The listing will serve to replace all prior versions of the claims in the application.*

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/26/02 has been entered.

Terminal Disclaimer

The terminal disclaimer filed on Paper NO:31, 02/24/03 disclaiming the terminal portion of any patent granted on this application which would extend beyond the expiration date of US 6395959 has been reviewed and is accepted. The terminal disclaimer has been recorded.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 94-119 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The scope of invention as claimed encompasses a transgenic mouse or a method of culturing cells thereof wherein the transgenic mouse and the cells comprises a nucleic acid sequence comprising a Group I intron encoded endonuclease recognition site selected from group consisting of I-SceIV site, ICsmI site, I-PanI site, I-SceII site, I-CeuI site, I-Ppoi site, I-SceIII site, I-CreI site, I-TevI site, I-TevII site, I-TevIII site and I-SceI site. At best the instant specification only disclosed nucleic acid sequences of SEQ ID NO: 17, 19, 21, 23, 25, 27, 29, 35, 37, 39 41 and 43 which are cleaved by I-SceI, I-SceIV, I-SceII, I-CeuI, I-PpoI, I-SceIII, I-CreI, I-CsmI, I-PanI, I-TevI, I-Tev-II and I-TevIII endonucleases respectively.

Applicant is referred to the Interim guidelines on *Written Description* published December 21, 1999 in the Federal Register, Vol. 64, No. 244, pp. 71427-71440. The disclosure of a single species is rarely, if ever, sufficient to describe a broad genus, particularly when the specification fails to describe the features of that genus, even in passing. (see In re Shokal

113USPQ283(CCPA1957); Purdue Pharma L. P. vs Faulding Inc. 56 USPQ2nd 1481 (CAFC 2000). In the instant case the specification only teaches SEQ ID NO: 17, 19, 21, 23, 25, 27, 29, 35, 37, 39 41 and 43, which are recognition sites for I-SceI, I-SceIV, I-SceII, I-CeuI, I-PpoI, I-SceIII, I-CreI, I-CsmI, I-PanI, I-TevI, I-Tev-II and I-TevIII endonuclease. Besides the nucleotides sequences of SEQ ID NO: 17, 19, 21, 23, 25, 27, 29, 35, 37, 39, 41 and 43 the specification fails to disclose any other nucleic acid sequences that can be cleaved with I-SceI, I-SceIV, I-SceII, I-CeuI, I-PpoI, I-SceIII, I-CreI, I-CsmI, I-PanI, I-TevI, I-Tev-II and I-TevIII endonucleases explicitly or implicitly as putatively claimed by the applicant.

The possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with *sufficient relevant identifying characteristics* (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *See, e.g., Pfaff v. WellsElectronics, Inc., 525 U.S. 55, 68, 119 S.Ct. 304, 312, 48 USPQ2d 1641, 1647 (1998); Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406; Amgen, Inc. v. Chugai Pharmaceutical, 927 F.2d 1200, 1206, 18 USPQ2d 1016, 1021 (Fed. Cir. 1991).* In claims to genetic material, generic statement such as "vertebrate insulin cDNA" or mammalian insulin cDNA," without more, is not adequate written description of claimed genus, since it does not distinguish genus from others except by function, and does not specifically define any of genes that fall within its definition, or describe structural features commonly possessed by members of genus that distinguish them from others; accordingly, naming type of material generally known to exist, in absence of knowledge as to what that material consists of, is not description of that material (*Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406).*

In the instant case the group I intron encoded endonuclease recognition sites has been defined only by a statement of endonuclease activity, which conveyed no distinguishing information about the identity of the claimed DNA sequence, such as its relevant structural or physical characteristics. The nucleic acid as claimed encompasses any and all variant of endonuclease sites to be discover by the claimed endonuclease activity. These variants also encompass conserved nucleotide sequences, which are considered germane to the endonuclease mediated cleavage specificity. At best the specification only disclosed the nucleotides sequences of SEQ ID NO: 17, 19, 21, 23, 25, 27, 29, 35, 37, 39, 41 and 43, however the specification fails to disclose any other nucleic acid sequences that can be cleaved with I-SceI, I-SceIV, I-SceII, I-CeuI, I-PpoI, I-SceIII, I-CreI, I-CsmI, I-PanI, I-TevI, I-Tev-II and I-TevIII endonucleases explicitly or implicitly. According to these facts, one skill in the art would conclude that applicant was not in the possession of the claimed genus because a description of only one member of this genus is not representative of the variants of genus and is insufficient to support the claim.

2. Claims 94-119 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a transgenic mouse whose germ cells and somatic cells comprise an exogenous nucleic acid encoding a group I intron encoded endonuclease recognition site selected from a group consisting of nucleotides of SEQ ID NO: 17, 19, 21, 23, 25, 27, 29, 35, 37, 39 41 and 43, wherein the nucleotide sequences is recognized by I-SceI, I-SceIV, I-SceII, I-CeuI, I-PpoI, I-SceIII, I-CreI, I-CsmI, I-PanI, I-TevI, I-Tev-II and I-TevIII endonucleases

respectively, does not reasonably provide enablement for any transgenic mouse or cell obtained thereof which comprises a nucleic acid sequence *(other than the SEQ ID NO: 17, 19, 21, 23, 25, 27, 29, 35, 37, 39 41 and 43)* cleaved by I-SceI, I-SceIV, I-SceII, I-CeuI, I-PpoI, I-SceIII, I-CreI, I-CsmI, I-PanI, I-TevI, I-Tev-II or I-TevIII endonucleases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Nature Of Invention:

The invention as claimed relates to a transgenic mouse whose germ and somatic cells comprises an endonuclease site selected from group I intron encoded endonuclease sites comprising I-SceI, I-SceIV, I-SceII, I-CeuI, I-PpoI, I-SceIII, I-CreI, I-CsmI, I-PanI, I-TevI, I-Tev-II and I-TevIII sites

Breadth Of Claims And Guidance Provided By The Inventor:

The scope of invention as claimed encompasses a transgenic mouse and a method of culturing transgenic cells, wherein the transgene comprises a nucleotide sequences recognized by I-SceI, I-SceIV, I-SceII, I-CeuI, I-PpoI, I-SceIII, I-CreI, I-CsmI, I-PanI, I-TevI, I-Tev-II and I-TevIII endonucleases. At best the specification only disclosed that SEQ ID NO: 17, 19, 21, 23, 25, 27, 29, 35, 37, 39 41 and 43 which are the nucleotide sequences recognized by I-SceI, I-SceIV, I-SceII, I-CeuI, I-PpoI, I-SceIII, I-CreI, I-CsmI, I-PanI, I-TevI, I-Tev-II and I-TevIII endonucleases respectively. The instant specification fails to disclose any nucleic acid sequence (other than that SEQ ID NO: 17, 19, 21, 23, 25, 27, 29, 35, 37, 39 41 or 43) that is recognized by the I-SceI, I-SceIV, I-SceII, I-CeuI, I-PpoI, I-SceIII, I-CreI, I-CsmI, I-PanI, I-TevI, I-Tev-II or I-TevIII endonucleases respectively.

State Of Art And Predictability:

The stat of art regarding restriction endonucleases teaches that homing endonucleases are rare-cutting enzymes encoded by introns and inteins. They have striking structural and functional properties that distinguish them from restriction enzymes. Furthermore these enzymes make sites specific double-strand break that create recombinogenic ends, which engage in a gene conversion process that duplicates the intron or intein. Belfort et al, Nucleic Acids Res. 25 (17): 3379–3388 1997; see abstract, page 3379, col.1-2). Furthermore, length and degeneracy for many of these sites remains to be determined (page 3382, table-3). On the other hand it is not certain that degeneracy would certainly lead to the endonuclease specificity. For example yeast maturase, which are intron encoded LAGLIDADG proteins are thought to be degenerate endonucleases, they often have no demonstrable DNA cleavage activity (page 3381 col.1). In instant case the applicant fails to disclose that any variation in the claimed I-SceI, I-SceIV, I-SceII, I-CeuI, I-PpoI, I-SceIII, I-CreI, I-CsmI, I-PanI, I-TevI, I-Tev-II or I-TevIII recognition sites that would impart the endonuclease specific recognition and/or cleavage activity.

Quantity Of Experimentation Required:

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). In instant case screening of any and all degenerate variants of endonuclease sites for I-SceI, I-SceIV, I-SceII, I-CeuI, I-PpoI, I-SceIII, I-CreI, I-CsmI, I-PanI, I-TevI, I-Tev-II or I-TevIII over the entire length of recognition sequences is not considered routine in the art. Making and testing a point mutation is significantly different from the making and testing changes over entire length of recognition sequences wherein any and all nucleic acid residues are added, deleted and/or substituted. The number of possible

scenario increase geometrically with increase in percent non-identity. Such making and testing is nothing more than an invitation to further experimentation, since the specification can not be relied upon to teach how to make the variants as claimed. One has to engage in extensive making and testing in order to obtain variants that meet the requirements for the claimed I-SceI, I-SceIV, I-SceII, I-CeuI, I-PpoI, I-SceIII, I-CreI, I-CsmI, I-PanI, I-TevI, I-Tev-II or I-TevIII endonucleaase activity. This is not considered routine in the art and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). It is noted that the unpredictability of a particular area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Therefore, one skill in the art would have to engage in excessive and undue amount of experimentation to exercise the invention as claimed.

In addition, the invention as claimed recites "A transgenic mouse comprising a recombinant cell" (see scope of claim 94 and 107). Given the broadest reasonable interpretation the invention as claimed reads upon a transgenic mouse comprising a recombinant cell, wherein the transgene encoded in the transgenic mouse is different from the transgene present in the recombinant cell. For example invention as claimed read upon a transgenic mouse (any transgene), wherein the cell comprising an endonuclease site (as claimed) has been introduced via a method of gene delivery or cell transplantation. Therefore invention as claimed does not clearly read upon a transgenic mouse encoding a transgene comprising a nucleic acid encoding an endonuclease site (as claimed). At he time of filing the gene base delivery to any and all cells in vivo via any and all means has been considered highly unpredictable. Furthermore

transplantation of recombinant cells has also been considered unpredictable, since the scope of invention of as claimed encompasses a cell from any and all xenogenic organisms. The state of transgenic art at the time of filing teaches that transgenic animal are the animals whose somatic cells and germ cells comprises a transgene, wherein the animal is capable of passing the transgene to the offspring (see exhibit 3 and 4 attached to Paper No:22, filed by the applicant on 05/30/02).

Changing "A transgenic mouse comprising a recombinant cell, wherein said cell comprises a nucleotide sequence" to -- A transgenic mouse whose germ cells and somatic cell comprises an exogenous nucleotide sequence -- has been suggested.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claim 107-119 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 107 is indefinite because it is unclear what is considered "a unique location in a chromosome" in this context.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sumesh Kaushal Ph.D. whose telephone number is 703-305-6838. The examiner can normally be reached on Mon-Fri. from 9AM-5PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yucel Irem Ph.D. can be reached on 703-305-1998. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-8724 for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

S. Kaushal
PATENT EXAMINER

SUMESH KAUSHAL
PATENT EXAMINER